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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/170,344	03/30/1994	WYBE M. KAST	D45113TFM	4000

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 05/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/170,344	KAST ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,6,8,10,12,14,16 and 26-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6,8,10,12,14,16 and 26-30* is/are rejected.

7)☒ Claim(s) *5,6,8,10,12,14,16 and 26-30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 2 pgs.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendment filed March 1, 2006 is acknowledged and has been entered. Claims 1-4, 7, 9, 11, 13, 15 and 17-25 have been canceled. Claims 5, 6, 8, 10, 12, 14 and 16 have been amended. Claims 5, 6, 8, 10, 12, 14, 16 and 26-30 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment to the claims and/or comments with the exception of those discussed below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 5, 6, 8, 10, 12, 14, 16 and 26-30 are objected to because of the following informalities: see line 1 of claim 5, for example, the claim recites "...peptide have a length of from 9 to 12 amino acids..." the claims should be crafted to provide more clarity. For example, "...peptide comprising an amino acid sequence from 9 to 12 amino acids in length...". Claim 16, for example, "...composition comprising a peptide according to claim 5 and a pharmaceutically acceptable carrier..." Claims 27-30 should recite a "pharmaceutically acceptable carrier". It is noted that these are only suggestions and not a directive for Applicants to specifically amend the claims in the above manner. It should be noted that any and all amendments to claims should find support and enablement in the pending specification.

4. The objection to the specification and rejection of claims 5, 6, 8, 10, 12, 14, 16 and now new claims 29-30 under 35 USC 112, 1st paragraph (i.e. lack of an enabling disclosure) is maintained for the reasons of record. Applicants' arguments filed March 1, 2006 have been fully considered but they are not deemed to be persuasive.

This rejection is maintained because there are claims pending directed to a pharmaceutical composition. Claims 16 and 26-30 are directed to pharmaceutical compositions comprising a peptide and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant.

With regard to the claimed pharmaceutical composition, the specification does not teach how to use a the pharmaceutical composition containing an effective amount for eliciting cellular immune response of the peptide derived from E6 or E7 of HPV16 or HPV18 and a pharmaceutically acceptable carrier, diluent, excipient or adjuvant. The disclosure is enabled for nonapeptide sequences from the E6 or E7 genes of HPV16 or HPVI8, and MHC Class I molecules as specifically taught in the specification. The specification contemplates that the pharmaceutical compositions can be used for prevention, prophylaxis, therapy and treatment of cervical carcinoma and/or adenoma and other HPV-related, in particular HPV16- and/or HPV18-related diseases (see p. 3, l. 31-35). The specification states that the "novel peptides of the present invention are useful in pharmaceutical compositions, as screening tools and in the prevention, prophylaxis, therapy and treatment of HPV16- and/or HPVl8-induced diseases or other conditions which would benefit from inhibition of HPVl6 and/or HPVl8 infection." (see p. 4, l. 12-16) However, the specification does not teach how to use the claimed pharmaceutical composition in the treatment of HPV16- and/or

HPV18-induced diseases comprising administering the pharmaceutical composition to a subject. The only evidence provided in the specification is in vitro data showing induction of primary immune response against HPV peptides. The data shows that the peptides bind to MHC Class I alleles. It is noted that a when a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that use. In this case, the specification must teach enablement of a pharmaceutical use since the claim recites a pharmaceutical composition. A pharmaceutical use would be any use, other than as food, wherein a substance is used on or in the body to prevent, diagnose, alleviate, treat, or cure a disease in humans or animals. The following are examples of "pharmaceutical uses": administering vitamin supplements (preventing disease); using labeled antibodies for *in vivo* imaging (diagnosing disease); administering a substance to alleviate a symptom of a disease (alleviating or treating disease); and administering an antibiotic (curing bacterial infection). Thus, to enable a pharmaceutical use for a substance, the specification must teach how to use the substance, without undue experimentation, for the prevention, diagnosis, alleviation, treatment, or cure a disease in the animal or subject to which the substance is administered. The instant specification is not enabled for such a pharmaceutical composition. Applicants have asserted that the peptides that bind to MHC-I are by definition capable of eliciting a cellular response when present. This is inherent in the workings of the immune system and well known to one skilled in the pertinent art. An immune response is automatically triggered upon presentation of a peptide by MHC-I. However, inducing an immune response is not a pharmaceutical use since it does not appear that any disease (i.e. HPV16- or HPV18-related diseases) has been alleviated, treated or prevented. Administering the claimed peptides to a subject to

produce antibodies which are then collected and used in an assay to diagnose the presence of HPV16- or HPV18-related diseases does not provide enablement for the claim because using the compound merely to produce antibodies for collection and subsequent use is not a pharmaceutical use. The pharmaceutical use must occur within the animal or subject to which the compound is administered for the prevention, diagnosis, alleviation, treatment, or cure of disease. Further, such short peptides require immunogenic carriers to ensure an immune response. The claimed composition does not set forth the use of any carriers.

The specification has not provided sufficient evidence that the claimed pharmaceutical composition can be used for its intended purpose. Matlashewski et al. discloses that HPV18 proteins (E6 gene) maybe diagnostically useful since the proteins have been identified in specific human cancers, however the use of the pharmaceutical composition as claimed in this invention are not known in the art. Accordingly, amendment of the claims to what is supported in the specification or filing of evidence in the form of a Rule 1.132 declaration providing factual evidence supporting the broad range claims is suggested.

A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which it pertains to make and use the invention as of its filing date, In re Glass, 18 1 USPQ 31; 492 F2.d 1228 (CCPA1974). While the prior art setting may be mentioned in general terms, the essential novelty, the essence of the invention, must be described in such details, including proportions and techniques where necessary, as to enable those persons skilled in the art to make and utilize the invention.

Specific operative embodiments or examples of the invention must be set forth Examples and description should be of sufficient scope as to justify the scope

of the claims. Where the constitution and formula of a compound is stated only as probability and speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula. A disclosure involving a new chemical compound or composition must teach persons skilled in the art how to make the compound. Incomplete teachings may not be completed by reference to subsequently filed applications.

The instant specification invites the skilled artisan to experiment. The factors, which must be considered in determining undue experimentation are set forth in Ex parte Forman 230 USPQ 546. The factors include 1) quantity of experimentation necessary, 2) the amount of guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the predictability of the art and the 7) breath of the claims. With regard to factors three and six, it is noted that there are no working examples or support for in vivo efficacy of the active ingredients in a pharmaceutical composition for therapeutic treatment of a human with cervical carcinoma or other HPV related diseases by administering a peptide from HPV proteins in a pharmaceutical composition, or peptides from any HPV that bind to MHC Class I molecules. Such is not seen as sufficient to support the breath of the claims, wherein the scope of the claims encompasses how to prepare a peptide from any of the listed HPV proteins (or any other HPV protein) wherein the peptide binds to any human MHC Class I molecule. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves., see In re Gardner et al. 166 USPQ 138 (CCPA 1970).

Applicants have argued that the specification is enabled and have cited Ruppert et al., Kast et al., Feltkamp et al., Vitiello et al., and Ressing et al. as support to demonstrate enablement, however it is noted that the specification must be enabled as of its filing date. Prior art references that were published after Applicants' effective filing date (5-5-92) cannot be used to rebut prima facie case of nonenablement under 35 USC 112. In re Glass, 181 USPQ 31; 492 F2.d 1228 (CCPA 1974).

Applicants have argued that it would be unethical to demonstrate HPV treatment in humans, however the Examiner has not suggested such a demonstration. Applicants have not demonstrated treatment of HPV in animal models. With regard to the therapeutic treatment, it appears that the specification is a paper protocol. The specification does not show any therapy or prophylactic treatment, only in vitro studies; no animal studies using the peptides to demonstrate prophylactic or therapy treatment that would correlate to human efficacy have been set forth in the specification. Applicants have argued that Kast et al. (PNAS, 1991, 88:2283-2287 and Immunol. Letters, 1991, 30(2):229-232) show that one of skill in the art would readily understand from these references how to make and use the claimed invention. Kast et al. (1991, PNAS) disclose the immunization of synthetic peptides of Sendai virus, not HPV. Further, Kast et al. (1991, Immunol. Letters) does disclose the use of peptide vaccination, however the use of HPV peptides is not discussed. HPV is discussed with regard to using "... cultured human CTL for immunotherapy of virus-induced tumors" (p. 229). Furthermore, the reference discloses that there are several unanswered questions regarding peptide vaccination as a novel immunotherapeutic or preventive approach in man (summary; p. 230, col. 2).

It is noted that the amendment filed March 1, 2006 deleted the "variant" language. However, the claims are still directed to pharmaceutical compositions and the specification does not provide enablement for a pharmaceutical composition. It is noted that Applicants did not set forth any arguments with regard to the claims directed to a pharmaceutical composition.

5. Claims 10, 12, 28 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Tindle et al (PNAS, July 1991, 88:5887-5891).

Tindle et al discloses peptides from E7 of HPV16 (abstract). Peptides from E7 of HPV16 are disclosed in Table 1 on p. 5888, Table 2 on p. 5890 and Figure 1. The B2 peptide disclosed in Table 1 is the same as claimed SEQ ID NO: 59. The peptide must be 9 to 12 amino acids in length and comprise an amino acid sequence derived from E7 of HPV16 as set forth in the specifically claimed sequences. The B2 peptide is 12 amino acids in length and discloses SEQ ID NO: 59 (HYNIVTFCC). Tindle et al discloses a pharmaceutical composition comprising the peptide and an adjuvant (materials and methods, p. 5888, col. 1).

It is noted that the claims recite a peptide comprising an amino acid sequence from a protein of E7 of HPV16. The prior art anticipates the claimed invention by disclosing a peptide from a HPV protein wherein the peptide binds to a MHC Class I allele HLA-A3.2, and a pharmaceutical composition. The peptides and compositions disclosed in Tindle et al are believed to inherently possess properties, which anticipates the claimed invention since the prior art peptides are from the same source, E7 of HPV16. With regard to claims 28 and 29, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish

the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey , 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963). See MPEP 2111.02 Further, products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Since the Office does not have the facilities for examining and comparing Applicants' HPV peptides and compositions and the HPV peptides and compositions of the prior art, the burden is on applicant to show a novel or unobvious differences between the claimed HPV peptides and compositions and the HPV peptides and compositions of the prior art (i.e., that the peptide and composition of the prior art does not possess the same material structural and functional characteristics of the claimed peptides and compositions). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald, 205 USPQ 594.

6. Claims 5 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Comerford et al (J. Virology, Sept. 1991, 65/9:4681-4690).

Comerford et al discloses T- and B-Cell epitopes of E7 of HPV 16 (title; abstract). Comerford et al discloses synthetic peptides from E7 of HPV16 in Figure 1, p. 4683. The claimed peptide must be 9 to 12 amino acids in length and

comprise an amino acid sequence derived from E7 of HPV16 as set forth in the specifically claimed sequences. Comerford et al discloses the peptide sequence of EYMLDLQPETT, which is 12 amino acids in length and discloses claimed SEQ ID NO: 14 (EYMLDLQPET). Comerford et al discloses a pharmaceutical composition comprising the peptide and pharmaceutically acceptable carrier (PBS) or an adjuvant (materials and methods, p. 4682, col. 1).

It is noted that the claims recite a peptide comprising an amino acid sequence from a protein of E7 of HPV16. The prior art anticipates the claimed invention by disclosing a peptide from a HPV protein wherein the peptide binds to a MHC Class I allele HLA-A2.1, and a pharmaceutical composition. The peptides and compositions disclosed in Comerford et al are believed to inherently possess properties, which anticipates the claimed invention since the prior art peptides are from the same source, E7 of HPV16. With regard to claim 16, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey , 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963). See MPEP 2111.02 Further, products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Since the Office does not have the facilities for examining and comparing Applicants' HPV peptides and compositions and the HPV peptides and compositions of the prior art, the burden is on applicant to show a novel or unobvious differences between the claimed HPV peptides and compositions and the HPV peptides and compositions of the prior art (i.e., that the peptide and composition of the prior art does not possess the same material structural and functional characteristics of the claimed peptides and compositions). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald, 205 USPQ 594.

7. No claims are allowed.

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
May 11, 2006